

FILE 'USPAT' ENTERED AT 16:23:34 ON 13 MAY
1999

* * * * * U. S. P A T E N T T E X T F
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* FILE *

* THE WEEKLY PATENT TEXT AND IMAGE DATA IS
CURRENT *
* THROUGH May 11, 1999.

\rightarrow a estrogen? (5a) receptor?

4724 ESTFCGEN?
38183 FECHETOR?
L1 934 ESTFCGEN? (5A) FECHETOR?

\Rightarrow still and shiny!

5343 CHIMER? 131 LI ANI CHIMER?

=> s 12 and orphan?

L3 B77 ORPHAN?
 L4 L7 AN ORPHAN?

$$\Rightarrow d = 1 - 24$$

1. 5,891,700, Apr. 4, 1999, Receptor-type phosphotyrosine phosphatases. gamma.; Joseph Schlessinger, 4/5/196 [IMAGE AVAILABLE]

2. 5,877,207, Mar. 1, 1999, Synthesis and use of retinoid compounds having negative hormone and/or antagonist activities; Elliott S. Klein, et al., 514,456; 549,405 [IMAGE AVAILABLE]

3. 5,876,981, Mar. 1, 1999, Yeast cells
engineered to produce pheromone
system protein surrogates and uses therefor;
Dana M. Powles, et al.,
4357/31, 254.11, 254.2, 254.21 (IMAGE
AVAILABLE)

4. 5,374,544, Feb. 23, 1999, Mutated steroid
hormone receptors, methods
for their use and molecular switch for gene
therapy; Elisabetta Vegetti,
et al., 520 350; 536/23.1, 24.1 [IMAGE
AVAILABLE]

5. 5,843,485, Iss. 15, 1998, Liver enriched transcription factor; Frances M. Sladek, et al., 435/6; 536/24.1 [IMAGE AVAILABLE]

6. 5,834,213, Nov. 10, 1998, Screening system and assay for identifying compounds that regulate steroid and **orphan** receptors mediation of DNA

transcription; Bert W. O'Malley, et al.,
435/7.8, 6, 7.2, 6).1, 320.1;
53-123.1 IMAGE AVAILABLE

7. 5,789,184, Aug. 4, 1998, Yeast cells engineered to produce pheromone system protein surrogates, and uses therefor; Datta M., Fowkes, et al., 4-45 (7.31, 254.1), 254.2, 254.21 [IMAGE AVAILABLE]

8. 5,786,361, Jul. 28, 1993, Method of
treating Hormone independent
cancer; Arner, Frongen, et al., 514/280 [IMAGE
AVAILABLE]

9. 5,776,634, Jul. 7, 1998, Method of identifying negative hormone and/or antagonist activities; Elliott S. Klein, et al., 435/712, 7.1, 63.1, 320.1, 325 [IMAGE AVAILABLE]

1. S.756,448, May 26, 1998, Constitute
activator of retinoid (CAR)
receptor polypeptides; David D. Moore, et
al., #14/2; 435/63.1; 520/350
[IMAGE AVAILABLE]

11. 5,710,317, Jan. 20, 1998, DNA encoding a
constitutive activator
retinoic acid response (RAR) receptor; David
L. Moore, et al., 415:69-1,
3, 11, 254; 596/21.5 [IMAGE AVAILABLE]

12. 5,710,604, Jan. 20, 1998, Methods of
using novel steroid histone
orphan receptors; Ronald M. Evans, et al.,
436/6, 64.1, 69.4, 69.7,
320.1, 325; 520/350; 536/22.1 [IMAGE
EVA1;ABIE]

14. 8,707,400, Jan. 13, 1968, Retinoic acid response elements and assays employing same; David John Mangelsdorf, et al., 435/6, 7.2, 7.21, 7.8, 80.1, 326.1, 325, 349, 358, 367; 536/23.1, 53.2 [IMAGE AVAILABLE]

14. 5,096,131, Dec. 9, 1977, **Orphan steroid hormone receptors;**
Finaldi M. Evans, et al., 500/350, 358 [IMAGE AVAILABLE]

15. 5,636,174, Nov. 11, 1997, Constitutive
activator of retinoic acid
receptor-receptor fusion protein; David
B. Miori, et al., 636/28C;
4-5/93.1, 636, 536/127.4 [IMAGE AVAILABLE]

17. 5-179, 518, Oct. 21, 1997, Method for
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activators of the NEF steroid hormone
receptor; Ethan Friedman, et al.,
4/5/c, 7.1 [IMAGE AVAILABLE]

17. S, #39,616, Jun. 17, 1997, Isolated nucleic acid encoding a ubiquitous nuclear receptor; Shutsung Liac, et al., 435/7.1, 69.1, 252.3, 320.1; #36/23.5, 24.3 [IMAGE AVAILABLE]

18. 5,607,967, Mar. 4, 1997, Treatment of alzheimer's disease with

5-(4-tridecyl-xylo)- β -furan carboxylic acid; Eitan Friedman, et al., 514/461, 473 [IMAGE AVAILABLE]

10. 5,604,115, Feb. 18, 1997, Liver enriched transcription factor; Frances M. Sladek, et al., 435/69.1, 252.3, 154.11, 320.1, 326, 348; 536/23.5 [IMAGE AVAILABLE]

11. 5,602,009, Feb. 11, 1997, Dominant negative **chimeras** of the steroid/thyroid superfamily of receptors; Ronald M. Evans, et al., 435/69.7, 252.3, 320.1; 530/350; 536/23.4 [IMAGE AVAILABLE]

12. 5,537,695, Jan. 28, 1997, Hormone response element compositions and assay; Ronald M. Evans, et al., 435/6, 69.7; 530/350, 350 [IMAGE AVAILABLE]

13. 5,566,956, Sep. 17, 1996, Methods and compositions relating to the androgen receptor gene and uses thereof; Arun K. Ray, et al., 436/24.1, 15.1, 24.3, 24.31 [IMAGE AVAILABLE]

14. 5,530,123, Jul. 2, 1996, Receptor-type phosphorylase; Joseph Schlessinger, 435/6, 69.1, 69.7, 70.1, 71.2, 166, 251.3, 254.1, 320.1, 357, 365; 536/23.1, 23.2 [IMAGE AVAILABLE]

15. 5,364,791, Nov. 15, 1994, Progesterone receptor having C-terminal furine binding domain truncations; Elisabetta Vegetti, et al., 435/320.1, 15.1; 530/350; 536/23.1 [IMAGE AVAILABLE]

... d 14 items

US PAT NO: 5,696,233 [IMAGE AVAILABLE]
D : 14 of 24

CLAIMS:

CLMS. 1)

That which is claimed is:

1. A polypeptide characterized by having a DNA binding domain comprising about 66 amino acids with 6 Cys residues, wherein said DNA binding domain is further characterized by the following amino acid sequence identity, relative to the DNA binding domains of hRAR-alpha, hTR-beta, hGR and hRXR-alpha, respectively:
A. (i) about 63% amino acid sequence identity with the DNA binding domain of hRAR-alpha;
(ii) about 59% amino acid sequence identity with the DNA binding domain of hTR-beta;
(iii) about 44% amino acid sequence identity with the DNA binding domain of hGR; and
(iv) about 65% amino acid sequence identity with the DNA binding domain

of hRXR-alpha; or
B. (i) about 55% amino acid sequence identity with the DNA binding domain of hRAF-alpha;
(ii) about 54% amino acid sequence identity with the DNA binding domain of hTF-beta;
(iii) about 50% amino acid sequence identity with the DNA binding domain of hGF; and
(iv) about 53% amino acid sequence identity with the DNA binding domain of hRXR-alpha; or
C. (i) about 61% amino acid sequence identity with the DNA binding domain of hRAF-alpha;
(ii) about 58% amino acid sequence identity with the DNA binding domain of hTR-beta;
(iii) about 47% amino acid sequence identity with the DNA binding domain of hGF; and
(iv) about 62% amino acid sequence identity with the DNA binding domain of hRXR-alpha; or
D. (i) about 58% amino acid sequence identity with the DNA binding domain of hRAF-alpha;
(ii) about 52% amino acid sequence identity with the DNA binding domain of hTR-beta;
(iii) about 44% amino acid sequence identity with the DNA binding domain of hGF; and
(iv) about 61% amino acid sequence identity with the DNA binding domain of hRXR-alpha; or
E. (i) about 53% amino acid sequence identity with the DNA binding domain of hRAR-alpha;
(ii) about 54% amino acid sequence identity with the DNA binding domain of hTR-beta;
(iii) about 45% amino acid sequence identity with the DNA binding domain of hGF; and
(iv) about 63% amino acid sequence identity with the DNA binding domain of hRXR-alpha.

CLMS(2)

2. A polypeptide according to claim 1 wherein the DNA binding domain of said polypeptide has:
(i) about 64% amino acid sequence identity with the DNA binding domain of hRAF-alpha;
(ii) about 56% amino acid sequence identity with the DNA binding domain of hTF-beta;
(iii) about 45% amino acid sequence identity with the DNA binding domain of hGR; and
(iv) about 61% amino acid sequence identity with the DNA binding domain of hRXR-alpha.

CLMS(3)

3. A polypeptide according to claim 2 wherein the ligand binding domain of said polypeptide has:
(i) about 27% amino acid sequence identity with the ligand binding

i) main of hRAR-alpha;
ii) about 58% amino acid sequence identity with the ligand binding domain of hTR-beta;
iii) about 10% amino acid sequence identity with the ligand binding domain of hGR; and
iv) about 22% amino acid sequence identity with the ligand binding domain of hRXR-alpha.

CLMS(4):

4. A polypeptide according to claim 3 wherein said polypeptide has an overall amino acid sequence identity of:
(i) about 32% relative to hRAR-alpha;
(ii) about 31% relative to hTR-beta;
(iii) about 18% relative to hGR; and
(iv) about 29% relative to hRXR-alpha.

CLMS(5):

5. A polypeptide according to claim 1 wherein the DNA binding domain of said polypeptide has:
(i) about 55% amino acid sequence identity with the DNA binding domain of hRAR-alpha;
(ii) about 55% amino acid sequence identity with the DNA binding domain of hTR-beta;
(iii) about 5% amino acid sequence identity with the DNA binding domain of hGR; and
(iv) about 52% amino acid sequence identity with the DNA binding domain of hRXR-alpha.

CLMS(6):

6. A polypeptide according to claim 5 wherein the ligand binding domain of said polypeptide has:
(i) about 32% amino acid sequence identity with the ligand binding domain of hRAR-alpha;
(ii) about 29% amino acid sequence identity with the ligand binding domain of hTR-beta;
(iii) about 20% amino acid sequence identity with the ligand binding domain of hGR; and
(iv) about 13% amino acid sequence identity with the ligand binding domain of hRXR-alpha.

CLMS(7):

7. A polypeptide according to claim 6 wherein said polypeptide has an overall amino acid sequence identity of:
(i) about 38% relative to hRAR-alpha;
(ii) about 31% relative to hTR-beta;
(iii) about 24% relative to hGR; and
(iv) about 27% relative to hRXR-alpha.

CLMS(8):

8. A polypeptide according to claim 1 wherein the DNA binding domain of said polypeptide has:
(i) about 62% amino acid sequence identity with the DNA binding domain of hRAR-alpha;

(ii) about 58% amino acid sequence identity with the DNA binding domain of hTR-beta;
(iii) about 48% amino acid sequence identity with the DNA binding domain of hGR; and
(iv) about 62% amino acid sequence identity with the DNA binding domain of hRXR-alpha.

CLMS(9):

9. A polypeptide according to claim 8 wherein the ligand binding domain of said polypeptide has:
(i) about 19% amino acid sequence identity with the ligand binding domain of hRAR-alpha;
(ii) about 27% amino acid sequence identity with the ligand binding domain of hTR-beta;
(iii) about 21% amino acid sequence identity with the ligand binding domain of hGR; and
(iv) about 24% amino acid sequence identity with the ligand binding domain of hRXR-alpha.

CLMS(10):

10. A polypeptide according to claim 9 wherein said polypeptide has an overall amino acid sequence identity of:
(i) about 32% relative to hRAR-alpha;
(ii) about 31% relative to hTR-beta;
(iii) about 25% relative to hGR; and
(iv) about 33% relative to hRXR-alpha.

CLMS(11):

11. A polypeptide according to claim 1 wherein the DNA binding domain of said polypeptide has:
(i) about 59% amino acid sequence identity with the DNA binding domain of hRAR-alpha;
(ii) about 52% amino acid sequence identity with the DNA binding domain of hTR-beta;
(iii) about 14% amino acid sequence identity with the DNA binding domain of hGR; and
(iv) about 61% amino acid sequence identity with the DNA binding domain of hRXR-alpha.

CLMS(12):

12. A polypeptide according to claim 11 wherein the ligand binding domain of said polypeptide has:
(i) about 19% amino acid sequence identity with the ligand binding domain of hRAR-alpha;
(ii) about 21% amino acid sequence identity with the ligand binding domain of hTR-beta;
(iii) about 20% amino acid sequence identity with the ligand binding domain of hGR; and
(iv) about 27% amino acid sequence identity with the ligand binding domain of hRXR-alpha.

CLMS(13):

13. A polypeptide according to claim 12 wherein said polypeptide has an overall amino acid sequence identity of:
(i) about 22% relative to hRAR-alpha;
(ii) about 24% relative to hTR-beta;
(iii) about 18% relative to hGR; and
(iv) about 29% relative to hRXR-alpha.

CLMS(14)

14. A polypeptide according to claim 1 wherein the DNA binding domain of said polypeptide has:
(i) about 50% amino acid sequence identity with the DNA binding domain of hRAR-alpha;
(ii) about 95% amino acid sequence identity with the DNA binding domain of hTR-beta;
(iii) about 50% amino acid sequence identity with the DNA binding domain of hGR; and
(iv) about 65% amino acid sequence identity with the DNA binding domain of hRXR-alpha.

CLMS(15)

15. A polypeptide according to claim 14 wherein the ligand binding domain of said polypeptide has:
(i) about 18% amino acid sequence identity with the ligand binding domain of hRAR-alpha;
(ii) about 20% amino acid sequence identity with the ligand binding domain of hTR-beta;
(iii) about 20% amino acid sequence identity with the ligand binding domain of hGR; and
(iv) about 24% amino acid sequence identity with the ligand binding domain of hRXR-alpha.

CLMS(16)

16. A polypeptide according to claim 15 wherein said polypeptide has an overall amino acid sequence identity of:
(i) about 24% relative to hRAR-alpha;
(ii) about 28% relative to hTR-beta;
(iii) about 18% relative to hGR; and
(iv) about 33% relative to hRXR-alpha.

CLMS(17)

17. A polypeptide according to claim 1 wherein the ligand binding domain of said polypeptide is further characterized by the following amino acid sequence identity, relative to the ligand binding domains of hRAR-alpha, hTR-beta, hGR and hRXR-alpha, respectively:
A (i) about 27% amino acid sequence identity with the ligand binding domain of hRAR-alpha;
(ii) about 30% amino acid sequence identity with the ligand binding domain of hTR-beta;
(iii) about 20 amino acid sequence identity with the ligand binding domain of hGR; and
(iv) about 22% amino acid sequence identity with the ligand binding

domain of hRXR-alpha; or
B. (i) about 32% amino acid sequence identity with the ligand binding domain of hRAR-alpha;
(ii) about 29% amino acid sequence identity with the ligand binding domain of hTR-beta;
(iii) about 1% amino acid sequence identity with the ligand binding domain of hGR; and
(iv) about 23% amino acid sequence identity with the ligand binding domain of hRXR-alpha; or
C. (i) about 1% amino acid sequence identity with the ligand binding domain of hRXR-alpha;
(ii) about 24% amino acid sequence identity with the ligand binding domain of hTR-beta;
(iii) about 1% amino acid sequence identity with the ligand binding domain of hGR; and
(iv) about 24% amino acid sequence identity with the ligand binding domain of hRXR-alpha; or
D. (i) about 1% amino acid sequence identity with the ligand binding domain of hRAR-alpha;
(ii) about 24% amino acid sequence identity with the ligand binding domain of hTR-beta;
(iii) about 1% amino acid sequence identity with the ligand binding domain of hGR; and
(iv) about 24% amino acid sequence identity with the ligand binding domain of hRXR-alpha; or
E. (i) about 1% amino acid sequence identity with the ligand binding domain of hRXR-alpha;
(ii) about 24% amino acid sequence identity with the ligand binding domain of hTR-beta;
(iii) about 1% amino acid sequence identity with the ligand binding domain of hGR; and
(iv) about 24% amino acid sequence identity with the ligand binding domain of hRXR-alpha.

CLMS(18)

18. A polypeptide according to claim 1 wherein said polypeptide has an overall amino acid sequence identity, relative to hRAR-alpha, hTR-beta, hGR and hRXR-alpha, respectively of:

A. (i) about 1% relative to hRAR-alpha;
(ii) about 31% relative to hTR-beta;
(iii) about 14% relative to hGR; and
(iv) about 24% relative to hRXR-alpha; or
B. (i) about 1% relative to hRAR-alpha;
(ii) about 31% relative to hTR-beta;
(iii) about 14% relative to hGR; and
(iv) about 24% relative to hRXR-alpha; or
C. (i) about 1% relative to hRAR-alpha;
(ii) about 1% relative to hTR-beta;
(iii) about 1% relative to hGR; and
(iv) about 24% relative to hRXR-alpha; or
D. (i) about 1% relative to hRAR-alpha;
(ii) about 24% relative to hTR-beta;
(iii) about 1% relative to hGR; and
(iv) about 1% relative to hRXR-alpha; or
E. (i) about 1% relative to hRAR-alpha;
(ii) about 24% relative to hTR-beta;

11, 13, 15, 18 relative to SEQ ID NO: 1
19, 21, 23, 25 relative to RXR-alpha.

CLAIMS:

11. A polypeptide according to claim 1
wherein said polypeptide has the
same amino acid sequence as polypeptides
selected from SEQ ID NOS: 2, 4,
6, 8, 10, 12 or 14.

CLM(S)(10)

11. A **chimeric** receptor comprising an amino-terminal domain, a DNA-binding domain, and a ligand-binding domain,
wherein at least one of the domains thereof
is derived from the
polypeptide of claim 1; and
wherein at least one of the domains thereof
is derived from at least one
previously identified member of the
steroid/thyroid superfamily of
receptors.

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14 1 5696233/PN

>> s 11 and 14

15 1 L1 AND L4

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US PAT NO: 5,696,233 [IMAGE AVAILABLE]
EE: 1 of 1

SUMMARY:

RSUM(6)

A number of receptor proteins, each specific
for one of several classes
of cognate steroid hormones [e.g., **estrogens**
(estrogen receptor), progesterones (progesterone
receptor), glucocorticoid
(glucocorticoid receptor), androgens
(androgen receptor), aldosterones
(mineralocorticoid receptor), vitamin D
(vitamin D receptor)], retinoids
(e.g., retinoic acid receptor) or. . .

SUMMARY:

RSUM(11)

A . . . growth hormone genes, responsive
to glucocorticoids,
estrogens and thyroid hormones; the
transcriptional control units for
mammalian prolactin genes and progesterone
receptor genes, responsive
to **estrogens**; the transcriptional control
units for avian ovalbumin
genes, responsive to progesterones; mammalian
metallothionein gene
transcriptional control units, responsive to
glucocorticoids; . . .

PETPESC:

PETP(66)
wherein . . . least one previously
identified member of the
steroid/thyroid superfamily of receptors
e.g., glucocorticoid receptor
(GR), thyroid receptor (TR), retinoid-X
receptors (RAR),
mineralocorticoid receptor (MR), **estrogen**
receptor (ER),
the **estrogen related receptors** (e.g., hERK1
or hERK2), retinoid-X
receptors (e.g., RXR-alpha, RXR-beta, . . .
RXR-delta.), vitamin D
receptor (VDR), aldosterone receptor (AR),
progesterone. . .

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(FILE 'USPAT' ENTERED AT 16:23:34 ON 13
MAY 1999)
L1 934 S ESTROGEN?(5A)RECEPTOR?
L2 181 S L1 AND CHIMER?
L3 24 S L2 AND ORPHAN?
L4 1 S 5696233/PN
L5 1 S L1 AND L4